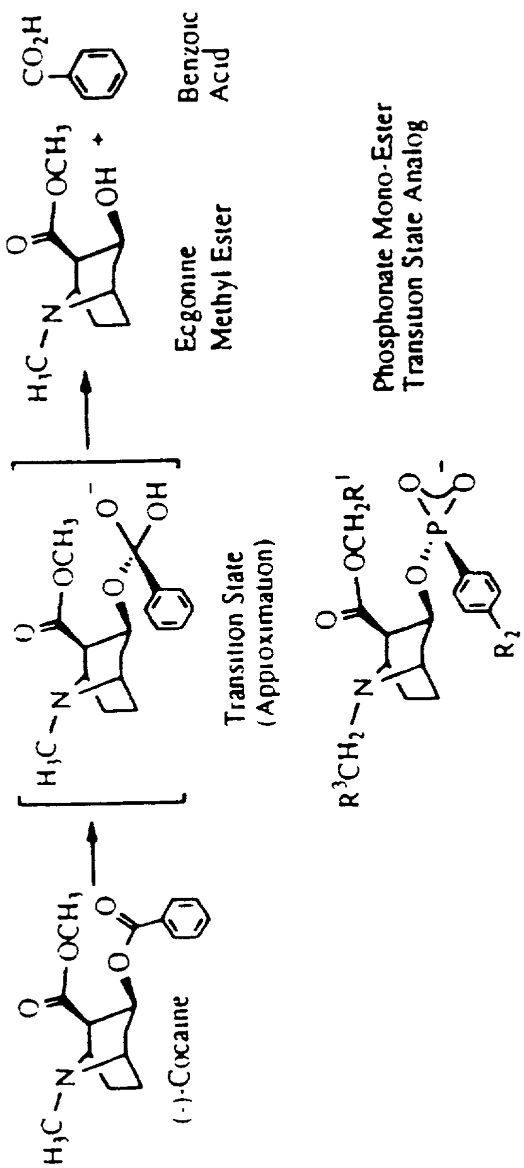
FIG. 1



TSA 1 $R^1 = (CH_2)_3NH^{14}CO(CH_2)_2{}^{14}CONH$–carrier protein; $R^2 = R^3 = H$
TSA 2 $R^2 = (CH_2)_3NH^{14}CO(CH_2)_2{}^{14}CONH$–carrier protein; $R^1 = R^3 = H$
TSA 3 $R^3 = (CH_2)_2NH^{14}CO(CH_2)_2{}^{14}CONH$–carrier protein; $R^2 = R^1 = H$
Free TSA 4 $R^1 = R^2 = R^3 = H$

FIG. 2

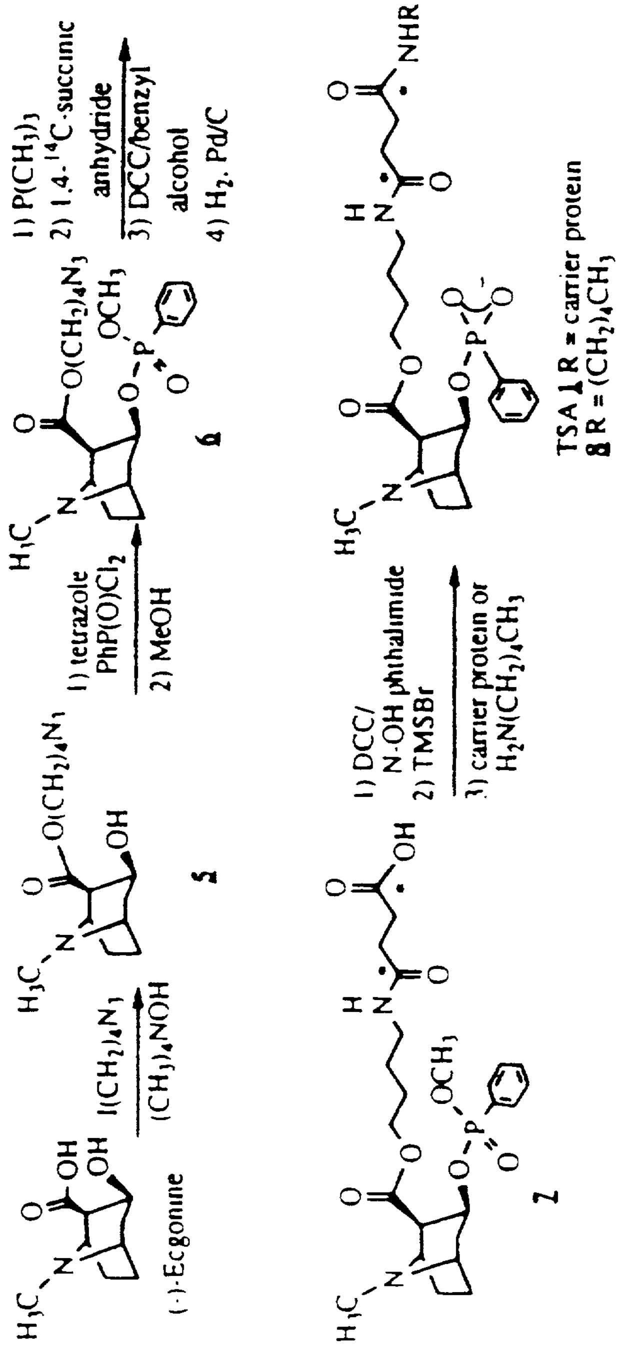

(-)-Ecgonine
$I(CH_2)_4N_3$
$(CH_3)_4NOH$
5
1) tetrazole
$PhP(O)Cl_2$
2) MeOH
6
1) $P(CH_3)_3$
2) 1,4-^{14}C-succinic anhydride
3) DCC/benzyl alcohol
4) H_2, Pd/C
7
1) DCC/ N-OH phthalimide
2) TMSBr
3) carrier protein or $H_2N(CH_2)_4CH_3$
TSA 1 R = carrier protein
8 R = $(CH_2)_4CH_3$

FIG. 3

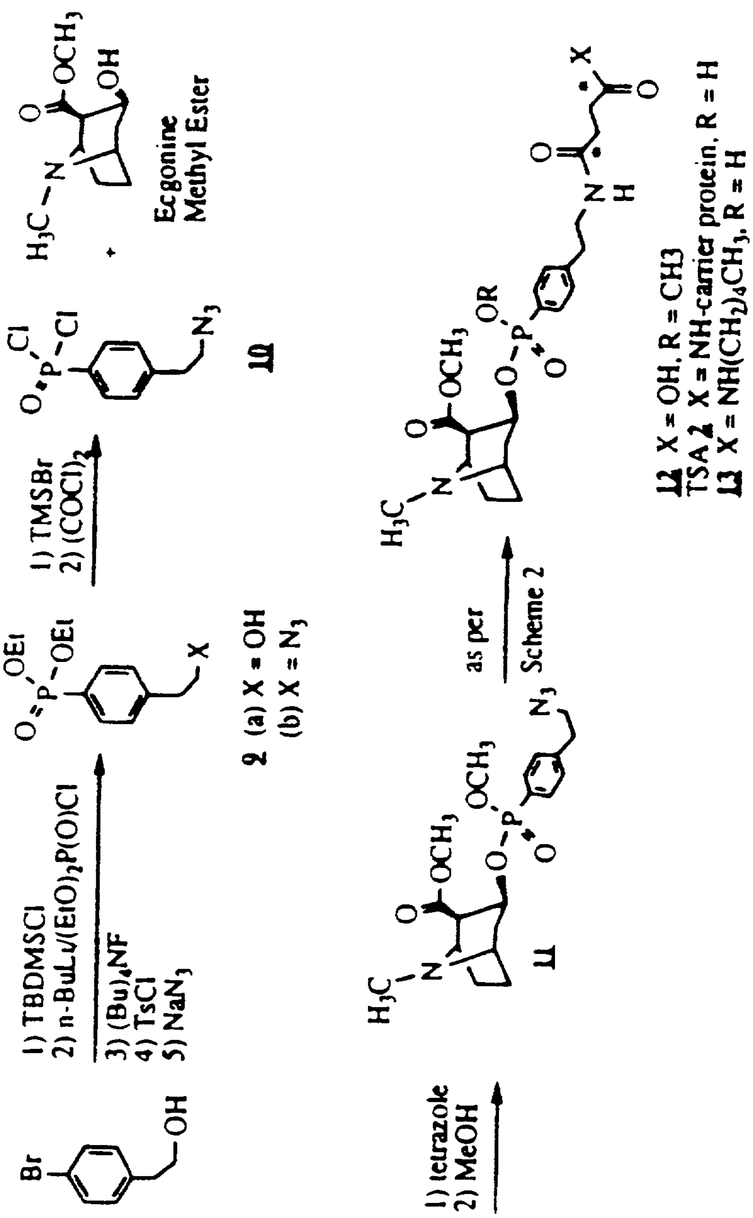

Br
OH
1) TBDMSCl
2) n-BuLi/(EtO)2P(O)Cl
3) (Bu)4NF
4) TsCl
5) NaN3
OEt
OEt
X
9 (a) X = OH
(b) X = N3
1) TMSBr
2) (COCl)2
Cl
Cl
N3
10
H3C
OCH3
OH
Ecgonine
Methyl Ester
1) tetrazole
2) MeOH
11
as per
Scheme 2
OR
12 X = OH, R = CH3
TSA 2 X = NH-carrier protein, R = H
13 X = NH(CH2)4CH3, R = H

FIG. 4

Scheme 4

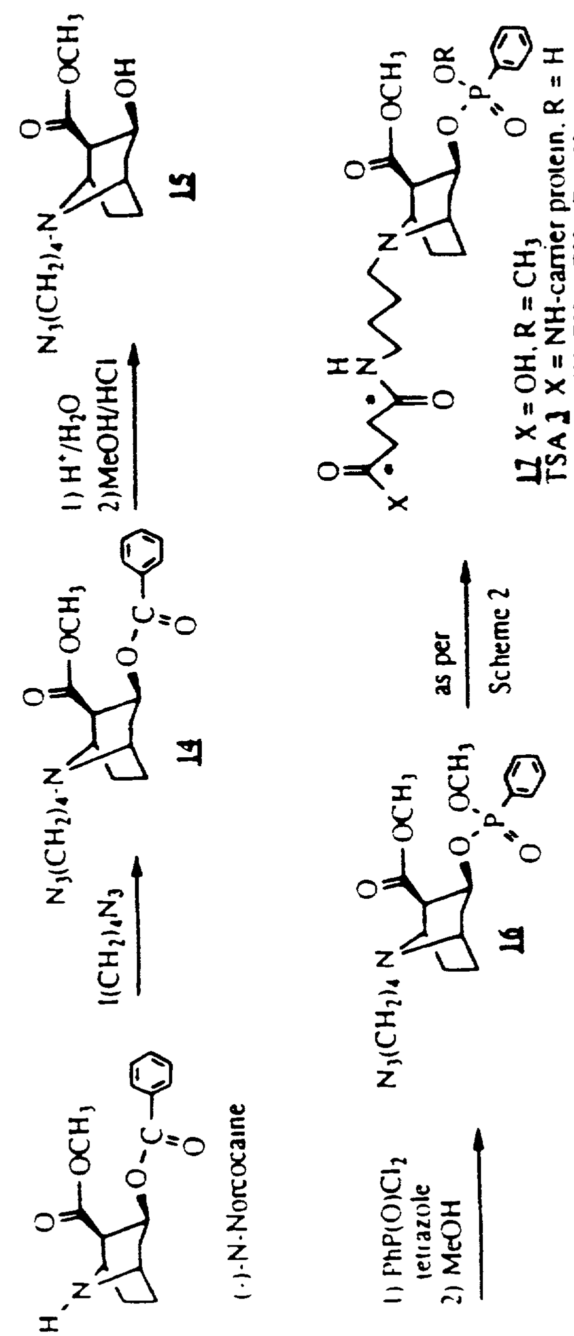


FIG. 5

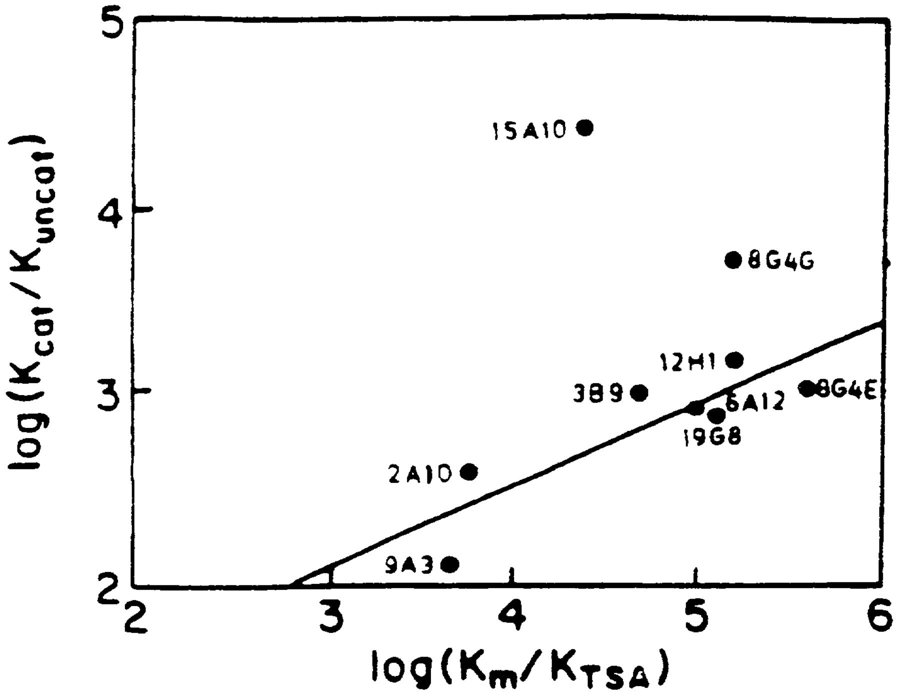

15A10
8G4G
12H1
3B9
6A12
8G4E
19G8
2A10
9A3
5
4
3
2
2
3
4
5
6
log(Kcat/Kuncat)
log(Km/KTSA)

FIG. 6

LAMBDA LIGHT CHAIN ALIGNMENT

```
9A(lam9) vari      1:----------TWPGETVTLTCRSSTGTITTSNYANWVQEKPDHLFSGLIGINNNRPPGVP
19G(lam5)  vari    1:----------.R............A.........................V.........
15A10L Vari        1:AVVTQESALT.S.................SD...................V..Y......
G7(lam4) vari      1:----------.RA...........S....AN..GS..........T....VS...G....
                               *  *********** ****  **  ********** ****  * * ****

9A(lam9) vari     61:ARFSGSLIGDKAVLTITGAQTEDEAIYFCALWYSNHWVFGGGTKLTVLG
19G(lam5)  vari   61:..........T.A....................................
15A10 Vari        61:.......T.........................................
G7(lam4) vari     61:..................G.............N...F............
                     ******* ** * ***** ************* *** ************
```

FIG. 7

KAPPA LIGHT CHAIN ALIGNMENT

```
3B9 K vari       1:DIVMTQDELSNPVTSGESVSISCRSSRSLLYRDGKTYLNWFLQRPGRSPQLLIYLMSTRS
6A12 k vari      1:.M.........................................................A
12H(L2) k vari   1:.M.........................................................A
2A k vari        1:...I......................K....E..............Q..H.........A
E2(L7) k Vari    1:EL....SP.TLS..I.QPA....K..Q....S.........F....Q..KR....V.KLD
                     * **  *   ** *   **** ** **** ********* **** **   **** *

3B9 K vari      61:SGVSDRFSGSGSGTDFTLEISRVKAEDVGVYYC-QHFVDYPFTFGSGTKLEIKR
6A12 k vari     61:.................................-...E................
12H(L2) k vari  61:.................................-....................
2A k vari       61:.............................A...-.Q..E.............R.
E2(L7) k Vari   61:...P...T.....K....K....E...L.L...V.GY-TF.L...A.....L..
                   *** *** ***** **** **** *** * *** *     * *** *****  *
```

FIG. 8

HEAVY CHAIN ALIGNMENT

```
3B9 vari       1:DVQLQESGPGLVKPSQSLSLTCTVTGNSITSDYAWTWIRQFPGNKLEWMGYIR-HIYGTR
6A12 heavy     1:.....................................................-......
12H H vari     1:.......................................K........L....-......
2AH-3 vari     1:---------E................Y........N........R........-YSGI..
9(H-3) vari    1:------...E....GA.VK.S.KAS.YPF.-..NMY.VK.SH.KS...I...DPSNG.IF
19h6-3 vari    1:EIH..Q...E....GA.VK.S.KAS.Y.F.-..NMY.VK.SH.KS...I...DP.NG.IF
15A10 vari     1:E........E....GA.VKVS.KAS.Y.F.-..NMY.VK.NH.ES...IA..DPSNGD.F
E2(H8) vari    1:VQL.E-..AE..M.GA.VKMS.KAS.YTF.-.HWMH.VK.R..QG...I.T.DLSDTY.G
G7(H8) Vari    1:VQL.E-..AE....GA.VE.S.RTS.YTF.-T.YIY.VK.R..QG...I.GMNPGNGV.Y
                           ** *  *    *   *   *      *     *  ***

3B9 vari      61:YNPSLISRISITRDTSKNQFFLQLDSVTAEDTATYYCVRYHYYGSAYWGQGTLVTVSA
6A12 heavy    61:..........................................................
12H H vari    61:..........................................................
2AH-3 vari    61:.....K............K.....N...T..........I....YGN.....TL.GLP
9(H-3) vari   61:..QKFKG.ATL.V.K.S.TA.MH.N.L.S..S.V...A.GGGL-F............E
19H6-3 vari   61:..QKFKG.ATL.V.K.S.TA.MH.N.L.S..S.V...A.GGGL-F....R........
15A10 vari    61:..QKFQGKATV.L.K.SSTA.MH.N.L.S..S.V...A.GGGL-F.F...........
E2(H8) vari   61:..QNFKG.ATL.L.E.S.TAYM..S.L.S..S.V...S.RG---FD......TL...S
G7(H8) Vari   61:F.EKFKN.ATL.V.R.SSIAYM..S.L.S..S.V...T.VGNL-F....R........
                  *         * * *       * * * ** * *** *        ** **  *
```

FIG. 9

```
         10        20        30        40        50        60
GCTGTTGTTACTCAGGAGTCTGCTCTAACTACATCACCTGGTGAAACAGTCACACTCACT
A  V  V  T  Q  E  S  A  L  T  T  S  P  G  E  T  V  T  L  T

         70        80        90       100       110       120
TGTCGCTCAAGTACTGGGACTATTACAAGTGATAACTATGCCAACTGGGTCCAAGAAAAA
C  R  S  S  T  G  T  I  T  S  D  N  Y  A  N  W  V  Q  E  K

        130       140       150       160       170       180
CCAGATCATTTATTCAGTGGTCTAATAGGTGTTAATAATTACCGACCTCCAGGTGTTCCT
P  D  H  L  F  S  G  L  I  G  V  N  N  Y  R  P  P  G  V  P

        190       200       210       220       230       240
GCCAGATTCTCAGGCTCCCTGACTGGAGACAAGGCTGTCCTCACCATCACAGGGGCACAG
A  R  F  S  G  S  L  T  G  D  K  A  V  L  T  I  T  G  A  Q

        250       260       270       280       290       300
ACTGAGGATGAGGCAATATATTTCTGTGCTCTATGGTACAGCAACCACTGGGTGTTCGGT
T  E  D  E  A  I  Y  F  C  A  L  W  Y  S  N  H  W  V  F  G

        310       320       330       340       350       360
GGAGGAACCAAACTGACTGTCCTAGGCCAGCCCAAGTCTTCGCCATCAGTCACCCTGTTT
G  G  T  K  L  T  V  L  G
```

FIG. 10

```
         10        20        30        40        50        60
TCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGGTATCCTGTAAGGCTTCTGGT
S  G  P  E  L  V  K  P  G  A  S  V  K  V  S  C  K  A  S  G

         70        80        90       100       110       120
TATTCATTCACTGACTACAATATGTACTGGGTGAAGCAGAACCATGGAGAGAGCCTTGAA
Y  S  F  T  D  Y  N  M  Y  W  V  K  Q  N  H  G  E  S  L  E

        130       140       150       160       170       180
TGGATTGCATATATTGATCCTTCCAATGGTGATACTTTCTACAACCAGAAATTCCAGGGC
W  I  A  Y  I  D  P  S  N  G  D  T  F  Y  N  Q  K  F  Q  G

        190       200       210       220       230       240
AAGGCCACAGTGACTCTTGACAAGTCCTCCAGTACAGCCTTCATGCATCTCAACAGCCTG
K  A  T  V  T  L  D  K  S  S  S  T  A  F  M  H  L  N  S  L

        250       260       270       280       290       300
ACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAGGGGGGGGCCTGTTTGCTTTCTGG
T  S  E  D  S  A  V  Y  Y  C  A  R  G  G  G  L  F  A  F  W

        310       320       330
GGGCAAGGGACTCTGGTCACTGTCTCTGCA
G  Q  G  T  L  V  T  V  S  A
```

FIG. 11

```
          10        20        30        40        50        60
GTCGCATGCTCCCGGNCGNCATGGNCGCGGGATTGGGAATTCCACGAGGCCGGGGGAGAC
                                            T  R  P  G  E  T

          70        80        90       100       110       120
AGTCACACTCACTTGTCGTTCAAGTGCTGGGACTATTACAACTAGTAACTATGCCAACTG
 V  T  L  T  C  R  S  S  A  G  T  I  T  T  S  N  Y  A  N  W

         130       140       150       160       170       180
GGTCCAAGAAAAACCAGATCATTTATTCAGTGGTCTAATAGGTGTTAACAACAACCGACC
 V  Q  E  K  P  D  H  L  F  S  G  L  I  G  V  N  N  N  R  P

         190       200       210       220       230       240
TCCAGGTGTTCCTGCCAGATTCTCAGGCTCCCTGATTGGAGACACGGCTGCCCTCACCAT
 P  G  V  P  A  R  F  S  G  S  L  I  G  D  T  A  A  L  T  I

         250       260       270       280       290       300
CACAGGGGCACAGACTGAGGATGAGGCAATATATTTCTGTGCTCTATGGTACAGCAACCA
 T  G  A  Q  T  E  D  E  A  I  Y  F  C  A  L  W  Y  S  N  H

         310       320       330       340       350       360
CTGGGTGTTCGGTGGAGGAACCAAACTGACTGTCCTAGGCCAGCCCAAGTCTTCGNCATC
 W  V  F  G  G  G  T  K  L  T  V  L  G
```

FIG. 12

```
         10        20        30        40        50        60
GAATTCGGCACGAGCAGGAACTACAGGTGTCCACTCTGAGATCCACCTGCAGCAGTCTGG
                                         E  I  H  L  Q  Q  S  G

         70        80        90       100       110       120
ACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGTTATCCTGCAAGGCTTCTGGTTACTC
 P  E  L  V  K  P  G  A  S  V  K  L  S  C  K  A  S  G  Y  S

        130       140       150       160       170       180
ATTCACTGACTACAACATGTACTGGGTGAAACAGAGCCATGGAAAGAGCCTTGAGTGGAT
 F  T  D  Y  N  M  Y  W  V  K  Q  S  H  G  K  S  L  E  W  I

        190       200       210       220       230       240
TGGATATATTGATCCTCACAATGGTGGTATTTTCTACAACCAGAAGTTCAAGGGCAGGGC
 G  Y  I  D  P  H  N  G  G  I  F  Y  N  Q  K  F  K  G  R  A

        250       260       270       280       290       300
CACATTGACTGTTGACAAGTCCTCCAACACAGCCTTCATGCATCTCAACAGCCTGACATC
 T  L  T  V  D  K  S  S  N  T  A  F  M  H  L  N  S  L  T  S

        310       320       330       340       350       360
TGAGGACTCTGCAGTCTATTACTGTGCAAGAGGGGGGGGCCTGTTTGCTTACTGGGGCCG
 E  D  S  A  V  Y  Y  C  A  R  G  G  G  L  F  A  Y  W  G  R

        370       380       390       400       410       420
AGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACACCCCCATCTGTCTATCCACTGGC
 G  T  L  V  T  V  S  A
```

FIG. 13

```
          10        20        30        40        50        60
GTCGCATGCTCCCGGNCGCCATGGNCGCGGGATTGGGAATTCCACGTGGCCGGGGGAGAC
                                              T  W  P  G  E  T

          70        80        90       100       110       120
AGTCACACTCACTTGTCGCTCAAGTACTGGGACTATTACAACTAGTAACTATGCCAACTG
 V  T  L  T  C  R  S  S  T  G  T  I  T  T  S  N  Y  A  N  W

         130       140       150       160       170       180
GGTCCAAGAAAAACCAGATCATTTATTCAGTGGTCTGATAGGTATTAACAACAACCGACC
 V  Q  E  K  P  D  H  L  F  S  G  L  I  G  I  N  N  N  R  P

         190       200       210       220       230       240
TCCAGGTGTTCCTGCCAGATTCTCAGGCTCCCTGATTGGAGACAAGGCTGTCCTCACCAT
 P  G  V  P  A  R  F  S  G  S  L  I  G  D  K  A  V  L  T  I

         250       260       270       280       290       300
CACAGGGGCACAGACTGAGGATGAGGCAATATATTTCTGTGCTCTATGGTACAGCAACCA
 T  G  A  Q  T  E  D  E  A  I  Y  F  C  A  L  W  Y  S  N  H

         310       320       330       340       350       360
CTGGGTGTTCGGTGGAGGAACCAAACTGACTGTCCTAGGCCAGCCCAAGTCTTCGNCATC
 W  V  F  G  G  G  T  K  L  T  V  L  G
```

FIG. 14

```
          70        80        90        100       110       120
GGTCCAGCTGCTCGAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGTTATC
                 S  G  P  E  L  V  K  P  G  A  S  V  K  L  S

         130       140       150       160       170       180
CTGCAAGGCTTCTGGTTACCCATTCACTGACTACAACATGTACTGGGTGAAGCAGAGCCA
 C  K  A  S  G  Y  P  F  T  D  Y  N  M  Y  W  V  K  Q  S  H

         190       200       210       220       230       240
TGGAAAGAGCCTTGAGTGGATTGGATATATTGATCCTTCCAATGGTGGTATTTTTTACAA
 G  K  S  L  E  W  I  G  Y  I  D  P  S  N  G  G  I  F  Y  N

         250       260       270       280       290       300
CCAGAAGTTCAAGGGCAGGGCCACATTGACTGTTGACAAGTCCTCCAACACAGCCTTCAT
 Q  K  F  K  G  R  A  T  L  T  V  D  K  S  S  N  T  A  F  M

         310       320       330       340       350       360
GCATCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAGGGGGGGG
 H  L  N  S  L  T  S  E  D  S  A  V  Y  Y  C  A  R  G  G  G

         370       380       390       400       410       420
CCTGTTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGAAGCCAAAACGAAACC
 L  F  A  Y  W  G  Q  G  T  L  V  T  V  S  E
```

FIG. 15

```
          70        80        90       100       110       120
AGGCGGCCGCACTAGTGATTGGGAATTCCACGAGGGCGGGGGAGACAGTCACACTCACTT
                              T  R  A  G  E  T  V  T  L  T  C

         130       140       150       160       170       180
GTCGCTCAAGTAGTGGGACTATTACAGCTAATAACTATGGCAGCTGGGTCCAGGAAAAGC
  R  S  S  S  G  T  I  T  A  N  N  Y  G  S  W  V  Q  E  K  P

         190       200       210       220       230       240
CAGATCATTTATTCACTGGTCTAATAGGTGTTAGCAACAACCGAGGTCCAGGTGTTCCTG
  D  H  L  F  T  G  L  I  G  V  S  N  N  R  G  P  G  V  P  A

         250       260       270       280       290       300
CCAGATTCTCAGGCTCCCTAATTGGAGACAAGGCTGTCCTCACCATCACGGGGGGGCAGA
  R  F  S  G  S  L  I  G  D  K  A  V  L  T  I  T  G  G  Q  T

         310       320       330       340       350       360
CTGAGGATGAGGCAATTTATTTCTGTGCTCTATGGAACAGCAACCATTTCGTGTTCGGTG
  E  D  E  A  I  Y  F  C  A  L  W  N  S  N  H  F  V  F  G  G

         370       380       390       400       410       420
GAGGAACCAAACTGACTGTCCTAGGGCAGACCAAGTCTTTCGGCATCAAGCACCCTGTTT
  G  T  K  L  T  V  L  G  Q
```

FIG. 16

```
          10        20        30        40        50        60
CCATTGGGCCCGACGTCGCATGCTCCCGGCCGCCATGGCCGCGGGATTAGGTCCAACTTC
                                                    V  Q  L  L

          70        80        90       100       110       120
TCGAGTCTGGGGCTGAACTGGTGAAGCCTGGGGCTTCAGTGGAGTTGTCCTGCAGGACTT
 E  S  G  A  E  L  V  K  P  G  A  S  V  E  L  S  C  R  T  S

         130       140       150       160       170       180
CTGGCTACACCTTCACCACCTACTATATTTACTGGGTAAAACAGAGGCCTGGACAAGGCC
 G  Y  T  F  T  T  Y  Y  I  Y  W  V  K  Q  R  P  G  Q  G  L

         190       200       210       220       230       240
TTGAGTGGATTGGGGGGATGAATCCTGGCAATGGTGTTACTTACTTCAATGAAAAATTCA
 E  W  I  G  G  M  N  P  G  N  G  V  T  Y  F  N  E  K  F  K

         250       260       270       280       290       300
AGAACAGGGCCACACTGACTGTGGACAGATCCTCCAGCATTGCCTACATGCAACTCAGCA
 N  R  A  T  L  T  V  D  R  S  S  S  I  A  Y  M  Q  L  S  S

         310       320       330       340       350       360
GCCTGACATCTGAGGACTCTGCGGTCTATTACTGTACACGGGTGGGTAACCTCTTTGCTT
 L  T  S  E  D  S  A  V  Y  Y  C  T  R  V  G  N  L  F  A  Y

         370       380       390       400       410       420
ACTGGGGCCGAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACACCCCACTTTCTAT
 W  G  R  G  T  L  V  T  V  S  A
```

FIG. 17

```
            10        20        30        40        50        60
GATATTGTGATGACCCAGGATGAACTCTCCAATCCTGTCACTTCTGGAGAATCAGTTTCC
D  I  V  M  T  Q  D  E  L  S  N  P  V  T  S  G  E  S  V  S

            70        80        90       100       110       120
ATCTCCTGCAGGTCTAGTAGGAGTCTCCTATATAGGGATGGGAAGACATACTTGAATTGG
I  S  C  R  S  S  R  S  L  L  Y  R  D  G  K  T  Y  L  N  W

           130       140       150       160       170       180
TTTCTGCAGAGACCAGGACGATCTCCTCAACTCCTGATCTATTTGATGTCCACCCGTTCA
F  L  Q  R  P  G  R  S  P  Q  L  L  I  Y  L  M  S  T  R  S

           190       200       210       220       230       240
TCAGGAGTCTCAGACCGGTTTAGTGGCAGTGGGTCAGGAACAGATTTCACCCTGGAAATC
S  G  V  S  D  R  F  S  G  S  G  S  G  T  D  F  T  L  E  I

           250       260       270       280       290       300
AGTAGAGTGAAGGCTGAGGATGTGGGTGTGTATTACTGTCAACACTTTGTAGACTATCCA
S  R  V  K  A  E  D  V  G  V  Y  Y  C  Q  H  F  V  D  Y  P

           310       320       330
TTCACGTTCGGCTCGGGGACAAAGTTGGAGATAAAACGG
F  T  F  G  S  G  T  K  L  E  I  K  R
```

FIG. 18

```
         10        20        30        40        50        60
GATGTGCAGCTTCAGGAGTCGGGACCTGGCCTGGTGAAACCTTCTCAGTCTCTGTCCCTC
D  V  Q  L  Q  E  S  G  P  G  L  V  K  P  S  Q  S  L  S  L

         70        80        90       100       110       120
ACCTGCACTGTCACTGGCAATTCAATCACCAGTGATTATGCCTGGACCTGGATCCGGCAG
T  C  T  V  T  G  N  S  I  T  S  D  Y  A  W  T  W  I  R  Q

        130       140       150       160       170       180
TTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAAGGCACATTTATGGCACTAGGTAC
F  P  G  N  K  L  E  W  M  G  Y  I  R  H  I  Y  G  T  R  Y

        190       200       210       220       230       240
AACCCTTCTCTCATAAGTCGAATCTCTATCACTCGAGACACGTCCAAGAACCAGTTCTTC
N  P  S  L  I  S  R  I  S  I  T  R  D  T  S  K  N  Q  F  F

        250       260       270       280       290       300
CTGCAGTTGGATTCTGTGACTGCTGAGGACACAGCCACATATTATTGTGTAAGATATCAT
L  Q  L  D  S  V  T  A  E  D  T  A  T  Y  Y  C  V  R  Y  H

        310       320       330       340       350       360
TACTACGGTTCGGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACG
Y  Y  G  S  A  Y  W  G  Q  G  T  L  V  T  V  S  A  A  K  T

ACACCC
T  P
```

FIG. 19

```
         10        20        30        40        50        60
GATATGGTGATGACGCAAGATGAACTCTCCAATCCTGTCACTTCTGGAGAATCAGTTTCC
D  M  V  M  T  Q  D  E  L  S  N  P  V  T  S  G  E  S  V  S

         70        80        90       100       110       120
ATCTCCTGCAGGTCTAGTAGGAGTCTCCTATATAGGGATGGGAAGACATACTTGAATTGG
I  S  C  R  S  S  R  S  L  L  Y  R  D  G  K  T  Y  L  N  W

        130       140       150       160       170       180
TTTCTGCAGAGACCAGGACGATCTCCTCAACTCCTGATCTATTTGATGTCCACCCGTGCA
F  L  Q  R  P  G  R  S  P  Q  L  L  I  Y  L  M  S  T  R  A

        190       200       210       220       230       240
TCAGGAGTCTCAGACCGGTTTAGTGGCAGTGGGTCAGGAACAGATTTCACCCTGGAAATC
S  G  V  S  D  R  F  S  G  S  G  S  G  T  D  F  T  L  E  I

        250       260       270       280       290       300
AGTAGAGTGAAGGCTGAGGATGTGGGTGTGTATTACTTTCAACACTTTGAAGACTATCCA
S  R  V  K  A  E  D  V  G  V  Y  Y  F  Q  H  F  E  D  Y  P

        310       320       330       340       350       360
TTCACGTTCGGCTCGGGGACAAAATTGGAGATAAAACGGGCTGATGCTGCACCAACTGTA
F  T  F  G  S  G  T  K  L  E  I  K  R

TCCATCTT
```

FIG. 20

```
              10         20         30         40         50         60
GACGTGCAGTTGCAGGAGTCGGGACCTGGCCTGGTGAAACCTTCTCAGTCTCTGTCCCTC
D  V  Q  L  Q  E  S  G  P  G  L  V  K  P  S  Q  S  L  S  L

              70         80         90        100        110        120
ACCTGCACTGTCACTGGCAATTCAATCACCAGTGATTATGCCTGGACCTGGATCCGGCAG
T  C  T  V  T  G  N  S  I  T  S  D  Y  A  W  T  W  I  R  Q

             130        140        150        160        170        180
TTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAAGGCACATTTATGGCACTAGGTAC
F  P  G  N  K  L  E  W  M  G  Y  I  R  H  I  Y  G  T  R  Y

             190        200        210        220        230        240
AACCCTTCTCTCATAAGTCGAATCTCTATCACTCGAGACACGTCCAAGAACCAGTTCTTC
N  P  S  L  I  S  R  I  S  I  T  R  D  T  S  K  N  Q  F  F

             250        260        270        280        290        300
CTGCAGTTGGATTCTGTGACTGCTGAGGACACAGCCACATATTATTGTGTAAGATATCAT
L  Q  L  D  S  V  T  A  E  D  T  A  T  Y  Y  C  V  R  Y  H

             310        320        330        340        350        360
TACTACGGTTCGGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACG
Y  Y  G  S  A  Y  W  G  Q  G  T  L  V  T  V  S  A  A  K  T

ACACCC
T  P
```

FIG. 21

```
         10        20        30        40        50        60
GATATGGTGATGACGCAAGACGAACTCTCCAATCCTGTCACTTCTGGAGAATCAGTTTCC
D  M  V  M  T  Q  D  E  L  S  N  P  V  T  S  G  E  S  V  S

         70        80        90       100       110       120
ATCTCCTGCAGGTCTAGTAAGAGTCTCCTATATGAGGATGGGAAGACATACTTGAATTGG
I  S  C  R  S  S  K  S  L  L  Y  E  D  G  K  T  Y  L  N  W

        130       140       150       160       170       180
TTTCTGCAGAGACCAGGACAATCTCCTCACCTCCTGATCTATTTGATGTCCACCCGTGCA
F  L  Q  R  P  G  Q  S  P  H  L  L  I  Y  L  M  S  T  R  A

        190       200       210       220       230       240
TCAGGAGTCTCAGACCGGTTTAGTGGCAGTGGGTCAGGAACAGATTTCACCCTGGAAATC
S  G  V  S  D  R  F  S  G  S  G  S  G  T  D  F  T  L  E  I

        250       260       270       280       290       300
AGTAGAGTGAAGGCTGAGGATGTGGGTGCGTATTACTGTCAACAATTTGTAGAGTATCCA
S  R  V  K  A  E  D  V  G  A  Y  Y  C  Q  Q  F  V  E  Y  P

        310       320       330       340       350       360
TTCACGTTCGGCTCGGGGACAAAGTTGGAAATAAGACGGGTTGATGCCGCACCAACTGTA
F  T  F  G  S  G  T  K  L  E  I  R  R

TCCATCTT
```

FIG. 22

```
        10        20        30        40        50        60
CATTGGGCCCACGTCGAATGNTCCCGGNCGNCATGGNCGNGGGATTGANAGGGGGNCGGA
                                                           E

        70        80        90       100       110       120
GCTGGTGAAGCCTTCTCAGTCTCTGTCCCTCACCTGCACTGTCACTGGCTACTCAATCAC
 L  V  K  P  S  Q  S  L  S  L  T  C  T  V  T  G  Y  S  I  T

       130       140       150       160       170       180
CAGTGATTATGCCTGGAACTGGATCCGGCAGTTTCCAGGAAACAGACTGGAGTGGATGGG
 S  D  Y  A  W  N  W  I  R  Q  F  P  G  N  R  L  E  W  M  G

       190       200       210       220       230       240
CTACATAAGGTACAGTGGTATCACTAGGTACAACCCATCTCTCAAAAGTCGAATCTCTAT
 Y  I  R  Y  S  G  I  T  R  Y  N  P  S  L  K  S  R  I  S  I

       250       260       270       280       290       300
CACTCGAGACACATCCAAGAACAAGTTCTTCCTGCAGTTAAATTCTGTGACTACTGAGGA
 T  R  D  T  S  K  N  K  F  F  L  Q  L  N  S  V  T  T  E  D

       310       320       330       340       350       360
CACAGCCACTTATTACTGTGTAAGAATTCATTACTACGGCTACGGCAACTGGGGGCAAGG
 T  A  T  Y  Y  C  V  R  I  H  Y  Y  G  Y  G  N  W  G  Q  G

       370       380       390       400       410       420
CACCACTCTCACAGGTCTTCCTCAAGAGTCTGGGAAGAAATCCCACCCATCTTCCCCACT
 T  T  L  T  G  L  P
```

FIG. 23

```
          10        20        30        40        50        60
NCCTTGGGCCGANGGCGCATGCTCCCGGCCGCCATGGCCGCGGGATTAGAGCGATATGGT
                                                      D  M  V

          70        80        90       100       110       120
GATGACGCAGGATGAACTCTCCAATCCTGTCACTTCTGGAGAATCAGTTTCCATCTCCTG
 M  T  Q  D  E  L  S  N  P  V  T  S  G  E  S  V  S  I  S  C

         130       140       150       160       170       180
CAGGTCTAGTAGGAGTCTCCTATATAGGGATGGGAAGACATACTTGAATTGGTTTCTGCA
 R  S  S  R  S  L  L  Y  R  D  G  K  T  Y  L  N  W  F  L  Q

         190       200       210       220       230       240
GAGACCAGGACGATCTCCTCAACTCCTGATCTATTTGATGTCCACCCGTGCATCAGGAGT
 R  P  G  R  S  P  Q  L  L  I  Y  L  M  S  T  R  A  S  G  V

         250       260       270       280       290       300
CTCAGACCGGTTTAGTGGCAGTGGGTCAGGAACAGATTTCACCCTGGAAATCAGTAGAGT
 S  D  R  F  S  G  S  G  S  G  T  D  F  T  L  E  I  S  R  V

         310       320       330       340       350       360
GAAGGCTGAGGATGTGGGTGTGTATTACTGTCAACACTTTGTAGACTATCCATTCACGTT
 K  A  E  D  V  G  V  Y  Y  C  Q  H  F  V  D  Y  P  F  T  F

         370       380       390       400       410       420
CGGCTCGGGGACAAAGTTGGAGATAAAACGGGTTGATGCTGNANCAACTGTATCCATCTT
 G  S  G  T  K  L  E  I  K  R
```

FIG. 24

```
         70        80        90       100       110       120
CTAGTGATTGCTCTAGAGCGACGTGCAGTTGCAGGAGTCGGGACCTGGACTGGTGAAACC
                    D  V  Q  L  Q  E  S  G  P  G  L  V  K  P

        130       140       150       160       170       180
TTCTCAGTCTCTGTCCCTCACCTGCACTGTCACTGGTAATTCAATCACCAGTGATTATGC
 S  Q  S  L  S  L  T  C  T  V  T  G  N  S  I  T  S  D  Y  A

        190       200       210       220       230       240
CTGGACCTGGATCCGGAAGTTTCCAGGAAACAAACTGGAGTGGTTGGGCTACATAAGGCA
 W  T  W  I  R  K  F  P  G  N  K  L  E  W  L  G  Y  I  R  H

        250       260       270       280       290       300
CATTTATGGCACTAGGTACAACCCTTCTCTCATAAGTCGAATCTCTATCACTCGAGACAC
 I  Y  G  T  R  Y  N  P  S  L  I  S  R  I  S  I  T  R  D  T

        310       320       330       340       350       360
GTCCAAGAACCAGTTCTTCCTGCAGTTGGATTCTGTGACTGCTGAGGACACAGCCACATA
 S  K  N  Q  F  F  L  Q  L  D  S  V  T  A  E  D  T  A  T  Y

        370       380       390       400       410       420
TTATTGTGTAAGATATCATTACTACGGGTCGGCTTACTGGGGGCAAGGGACTCTGGTCAC
 Y  C  V  R  Y  H  Y  Y  G  S  A  Y  W  G  Q  G  T  L  V  T

        430       440       450       460       470       480
TGTCTCTGCAGGCAAAACGANACCCCATCTGTCTATCCACTGGCCCCGGAACGCCGCCAG
 V  S  A
```

FIG. 25

```
          10        20        30        40        50        60
TTNAAGGCCCNGACGCCGCATAGCTCNCGGCCGCCATGGCCGNGGGATTCCAGTTCCGAG
                                                          E

          70        80        90       100       110       120
CTCGTGATGACACAGTCTCCACTCACTTTGTCGGTAACCATTGGACAACCAGCCTCTATC
L  V  M  T  Q  S  P  L  T  L  S  V  T  I  G  Q  P  A  S  I

         130       140       150       160       170       180
TCTTGCAAGTCAAGTCAGAGCCTCTTATATAGTGATGGAAAAACCTATTTGAATTGGTTC
S  C  K  S  S  Q  S  L  L  Y  S  D  G  K  T  Y  L  N  W  F

         190       200       210       220       230       240
TTCCAGAGGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTAAACTGGACTCT
F  Q  R  P  G  Q  S  P  K  R  L  I  Y  L  V  S  K  L  D  S

         250       260       270       280       290       300
GGAGTCCCTGACAGGTTCACTGGCAGTGGATCAGGAAAAGATTTTACACTGAAAATCAGC
G  V  P  D  R  F  T  G  S  G  S  G  K  D  F  T  L  K  I  S

         310       320       330       340       350       360
AGAGTGGAGGCTGAGGATTTGGGACTTTATTACTGCGTTCAAGGGTACACATTTCCGCTC
R  V  E  A  E  D  L  G  L  Y  Y  C  V  Q  G  Y  T  F  P  L

         370       380       390       400       410       420
ACGTTCGGTGCTGGGACCAAGCTGGAGCTGAAACGGGTGATGCTGACCAACTTGTTTCAT
T  F  G  A  G  T  K  L  E  L  K  R
```

FIG. 26

```
          10        20        30        40        50        60
TTGGGCCCGGACGTCGCATGCTCCCGGCCGCCATGGNCGNGGGATTAGGTCCAACTTCTC
                                                  V  Q  L  L

          70        80        90       100       110       120
GAGTCTGGGGCTGAGCTTGTGATGCCTGGGGCTTCAGTGAAGATGTCCTGCAAGGCTTCT
E  S  G  A  E  L  V  M  P  G  A  S  V  K  M  S  C  K  A  S

         130       140       150       160       170       180
GGCTACACATTCACTGACCACTGGATGCACTGGGTGAAGCAGAGGCCTGGACAAGGCCTT
G  Y  T  F  T  D  H  W  M  H  W  V  K  Q  R  P  G  Q  G  L

         190       200       210       220       230       240
GAGTGGATCGGAACGATTGATCTTTCTGATACTTATACTGGCTACAATCAAAACTTCAAG
E  W  I  G  T  I  D  L  S  D  T  Y  T  G  Y  N  Q  N  F  K

         250       260       270       280       290       300
GGCAGGGCCACATTGACTCTCGACGAATCCTCCAACACAGCCTACATGCAGCTCAGCAGC
G  R  A  T  L  T  L  D  E  S  S  N  T  A  Y  M  Q  L  S  S

         310       320       330       340       350       360
CTGACATCTGAGGACTCTGCGGTCTATTACTGTTCAAGAAGGGGCTTTGACTACTGGGGG
L  T  S  E  D  S  A  V  Y  Y  C  S  R  R  G  F  D  Y  W  G

         370       380       390       400       410       420
CAAGGCACCACTCTCACAGTCTCCTCAGGCAAAACGACAACCCCATCTTGTCTNTCCACT
Q  G  T  T  L  T  V  S  S
```

FIG. 27

```
NdeI                                                         H1
|MEVQLQESGPELVKPSQSLSLTCTVTGNSIT[SDYAWT]WIRQFP
                  H2
GNKLEWMG[YIRHIYGTRYNPSLIS]RISITRDTSKNQFFLQLDS
                                                       SphI
                   H3                                   |------linker
VTAEDTATYYCVR[YHYYGSAY]WGQGTLVTVSAGMQSGGGGSG
           NcoI
------------||                                              L1
GGGSGGAMDIVMTQDELSNPVTSGESVSISC[RSSRSLLYRDGK
                        L2
TYLN]WFLQRPGRPPQLLIY[LMSTRSS]GVSDRFSGSGSGTDFTL
                      L3
EISRVKAEDVGVYYC[QHFVDYPFT]FGSGTKLEIKRADGAPTVS
          Flag        6 x His
IFPPSLDYKDDDDKLEHHHHHH
```

FIG. 28A

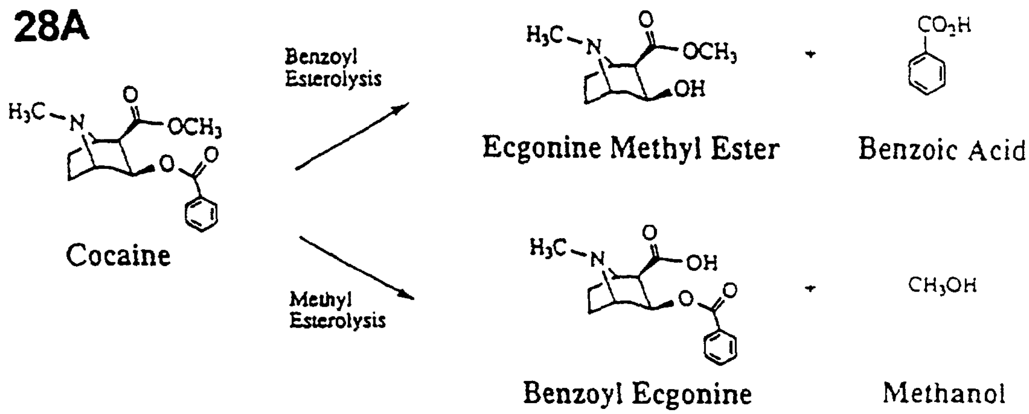


FIG. 28B

Transition State
Benzoyl Esterolysis
(Approximation)

Transition-State Analog
Free TSA R=H
TSA-I R=$(CH_2)_3NHCO(CH_2)_2CONH$-BSA

FIG. 29

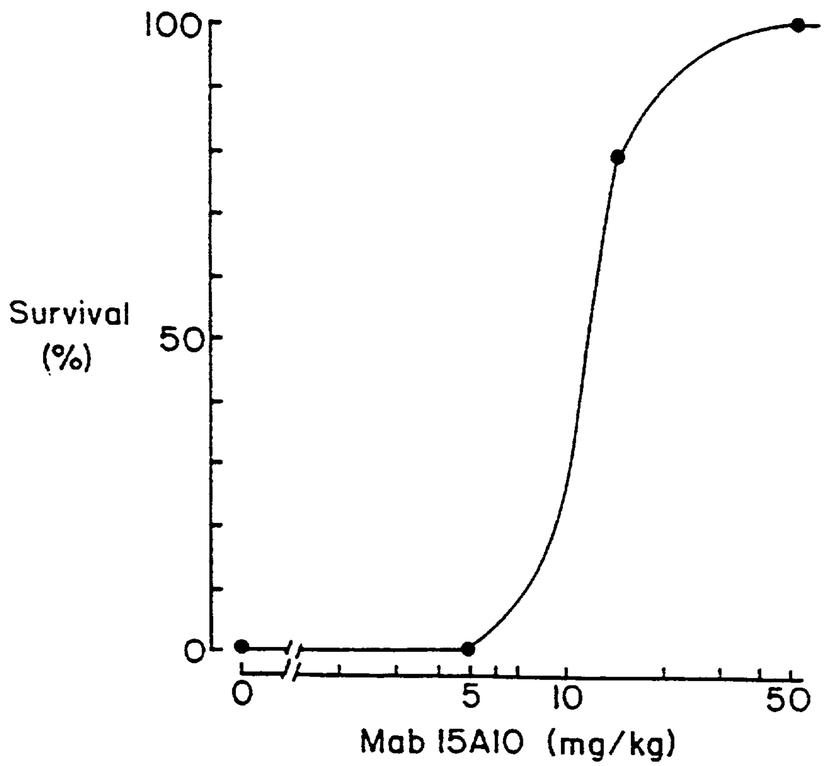


FIG. 30A

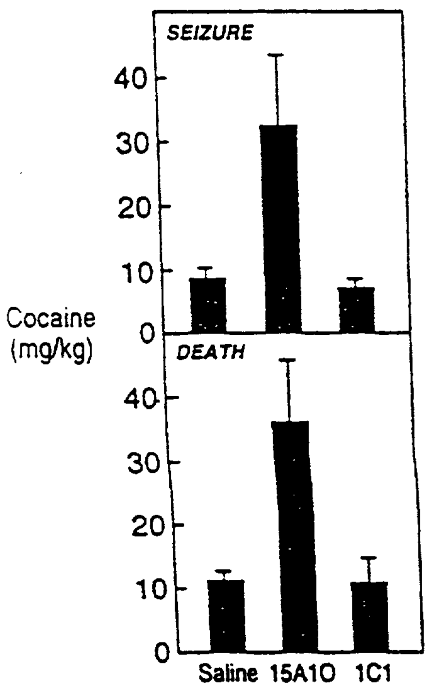


FIG. 30B

FIG. 30C

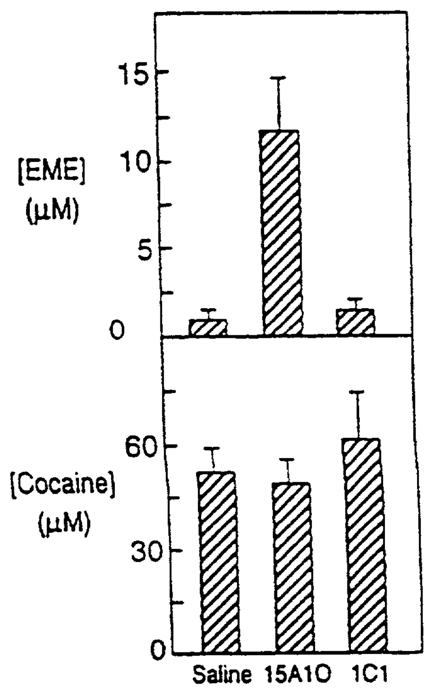


FIG. 30D